WS16.1 Clinical Outcomes of Real-World Kalydeco (CORK) study – Investigating the impact of CFTR potentiation on the intestinal microbiota, exocrine pancreatic function and intestinal inflammation prospectively over 12 months

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Objectives: Ivacaftor is effective in the treatment of patients with CF and the G551D gating mutation. We present faecal analysis results of the CORK cohort, a single-centre, adult (n = 20), prospective, longitudinal study of G551D clinical responders (median follow-up 12 months), examining the gut microbiota, exocrine pancreatic function and intestinal inflammation on a 3 monthly basis after commencing treatment.
Methods: Stool samples pre- and 3 monthly post commencement of ivacaftor in 20 adult patients underwent metagenomic profiling of faecal microbiota. Faecal elastase-1 (FE-1), faecal calprotectin (FC) and faecal lactoferrin (FL) were measured using commercially available ELISA kits.
Results: Ivacaftor did not significantly alter gut microbial diversity, as measured by chao1 ($p = 0.886$). At phylum, family and genus levels significant increases were observed in Bacteroidetes ($p = 0.044$), Bacteroidaceae ($p = 0.021$) and *Bacteroides* ($p = 0.021$). Significant decreases were observed in Microbacteriaceae ($p = 0.003$) and Eubacteriaceae ($p = 0.014$). A significant positive correlation was seen between FEV_1 and gut microbiota diversity following treatment ($r = 0.4$, $p = 0.002$). No significant difference was measured in levels of FE-1 ($p = 0.267$), FC ($p = 0.406$) or FL ($p = 0.779$).
Conclusion: Ivacaftor therapy has a normalisation effect on the gut microbiota, directing the microbiota towards a non-CF profile. Despite this elevated intestinal inflammation was sustained. Lack of exocrine pancreatic recovery may reflect established exocrine pancreatic dysfunction in an adult cohort. On-going longitudinal prospective data may demonstrate further improvements in the gut health of this cohort.

WS16.2 The prevalence of gastroesophageal reflux disease in infants with cystic fibrosis diagnosed by newborn screening and the relationship with lung infection

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Gastro-oesophageal reflux disease (GORD) has been implicated in the respiratory symptoms of CF. Studies in small populations suggest GORD may be present in up to 40% of these infants.
Aim: To describe the prevalence of GORD in a large cohort of infants with CF diagnosed by NBS. The secondary aim was to look for an association with bacterial infection.
Methods: Our NBS surveillance programme includes a 24 hr dual probe pH study and BAL for microbiology. Results were collected on infants over a 6 year period. GORD was diagnosed using ESPGHAN criteria: corrected reflux index (RI) >12%, reflux episodes >72, length of longest reflux episode >41 minutes. An association between GORD and positive bacterial samples was explored.
Results: Infants: n = 117, median age: 4.1 months (range 1.8–9.7 mo), 57 males (48%), 15 pancreatic insufficient (13%). 103 had valid pH studies (88%). RI >12% n = 44 (43%), reflux episodes >72 n = 55 (53%), reflux episodes >41 min n = 2. Positive bacteria at BAL = 29%. Including: PA = 3, SA = 8, HI = 5, coliforms = 7, other = 8 (some with mixed growths). There was no statistical difference in bacteria between those with and without GORD. There was a significant difference in wt z score –0.98 vs –0.2 $p < 0.02$. A scatter plot showed no significant reduction in RI with age.
Discussion: This large study confirms the high prevalence of GORD in infants with CF when using RI alone (43%), the true prevalence may be higher, 53% showed an abnormally high number of reflux episodes. No association with bacterial infection was found.
In conclusion: GORD appears more prevalent than thought in infants with CF and the significantly lower weight in this group needs further exploration.

WS16.3 Consecutive transient elastography measurements to detect cystic fibrosis liver disease

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Background: Cystic fibrosis (CF) related liver disease (CFLD) is diagnosed using a combination of criteria. Transient elastography (TE) (ultrasonographic method evaluating liver stiffness) differentiates CF patients with and without liver disease (CFnoLD) and identifies patients with an increased risk for portal hypertension.
Aim: Detect evolving CFLD using TE measurements.
Method: Retrospective study (2007–2013) including all patients with TE measurements, performed by the same operator. Measurement was correlated to the presence or development of CFLD based on the medical files.
Results: 150 CF patients [median age 17 (9–24) years] were included, 118 with repeated TE: 20 (14%) had CFLD at the first TE measurement, 4 (3%) developed CFLD during follow-up. The median TE value in CFLD was 14 (8.7–32.2) compared to 5.3 (4.9–5.7) in CFnoLD ($P = 0.0001$). The intra-individual differences between 2 consecutive measurements [median interval between measurements 1 yr (1–2)] was 0.05 (–1, 1.2) in CFnoLD and 0.55 (–1.68, 1.53) in the CFLD patients. The area under the receiver operating curve for TE predicting CFLD was 0.985. TE measurements above 6.55 kPa predicted CFLD with a sensitivity of 94.7% and a specificity of 90.8% according to the AUROC. In CF <14 years a TE measurement above 6.55 kPa had a positive predictive value of 83%, decreasing to 60% for the total group and a negative predictive value of 100%. Patients with developing CFLD had progressively increasing TE measurements.
Conclusion: TE measurements progressively increased in CF patients developing CFLD. A prospective study is needed to evaluate whether TE will be able to detect CFLD before it becomes clinically apparent.

WS16.4 Non invasive liver elastography (LSM) and computed tomography (CT) for evaluation of liver disease in 57 cystic fibrosis adult patients

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Objectives: Portal hypertension (PHT) is the main complication of cystic fibrosis liver disease (CFLD) but severe liver dysfunction occurred only in 0.5% of the patients. The early diagnosis of CFLD is elusive and a gold standard for diagnosis of liver disease is lacking. The aim of this study was to evaluate liver stiffness measurement (LSM) and CT with IV injected contrast medium in CF adult patients. Median LSM in 241 CF patients was 5.9 kPa.
Methods: 57 CF patients (28F, 33 yrs –18; 51) had LSM and CT done for lung transplant assessement or after lung transplantation.
Results: LSM was obtained in 53 patients (92%). PHT was evident on CT in 25 patients (portosystemic collaterals 12, splenomegaly 19, proeminent portal vein 25). PHT was present in 60% of the patients when LSM was >5.9 and in 12% when LSM was <5.9. None of the patients had variceal bleeding but 20/25 had screening for esophagal varices and 5 preventive variceal ligation (LSM 41.6, range 20–64). Nine patients had transient and easy to treat ascitis after lung transplantation. Only one patient (with good respiratory function) had refractory ascitis (LSM 64). Three patients received a combined lung and liver transplantation (LSM: 29/39/73 kPa). Explanted liver analysis disclosed absence of cirrhosis but obliterative portal venopathy.
Conclusion: CFLD with PHT could be present in patient with low LSM. Decompensation of PHT is unfrequent even in adults with end stage pulmonary disease or after lung transplantation. Portal venopathy without cirrhosis could explain PHT. The mechanism remains obscure but could explain the rare occurence of hepatocellular deficiency in CFLD.